Remarks

Applicant has carefully considered this Application in connection with the Examiner's Action, and respectfully requests reconsideration of this Application in view of the foregoing amendment, and the following remarks.

Applicant has added new Claim 18 and has amended Claims 4, 6, 8–11, 16 and 17, and cancels Claims 1–3, 5, 7 and 13–15. Accordingly, Claims 4, 6, 8–12, and 16–18 are presently pending in the Application, with Claims 16, 17 and 18 being the independent claims.

Applicant has amended sections VII and VIII below, in response to the Office Communication of 22 December 2008. As such, Applicant respectfully submits the corrected version of the response — in its entirety — to comply with 37 C.F.R. § 1.111.

I. Rejection of Claims 1-4, 6 and 13 under 35 U.S.C. § 102(b)

Claims 1-4, 6 and 13 are rejected by the Examiner under 35 U.S.C. § 102(b) as being anticipated by Katzhendler et al. (US 6,296,783). For the reasons discussed below, Applicant respectfully submits that the rejection is overcome.

The Examiner cites Katzhender for teaching the following:

- A controlled and sustained release oral drug delivery system comprising carbamazepine or a carbamazepine derivative. Carbamazepine or the derivative thereof is formulated within a polymeric matrix, said matrix optionally further containing additional pharmaceutically acceptable constituents and additives. The polymer in the polymeric matrix permits carbamazepine or its derivative to be released from the matrix by zero-order release kinetics (Col. 6, lines 21-29).
- Oxcarbazepine (10,11-dihydro-10-oxo-5H-dibenz/b,f/azepine-5-carboxamide) is disclosed as a carbamazepine derivative that is used as the pharmaceutically active agent in the drug delivery system (Col. 3, lines 57-63).

- The mono hydroxy derivative (MHD) of oxcarbazepine (10,11-dihydro-10-hydroxy-5H-dibenz/b,f/azepine-5-carboxamide) is also disclosed (Col. 3, lines 64-65).
- The polymer component of the drug delivery system comprises at least one hydrophilic polymer (Col. 8, lines 23-26) such as hydrophilic cellulose derivatives (Col. 8, lines 41-43).
- Hydroxypropyl methylcellulose (HPMC) is disclosed as a preferred hydrophilic cellulose derivative (Col. 8, lines 52-54).
- "Polymers are mixed with drug in a weight ratio of polymer to drug from about 1:99% to about 99:1%, preferably from about 5:95% to about 90:10%, most preferably from about 10:90% to about 80:20%, depending on the viscosity grade of the polymer, on the tablet dimension and shape and on the desired release rate" (Col. 8, lines 30-35).
- The erodible tablet form of the drug/matrix is disclosed (Col. 9, lines 25-27).
- The ratio of "drug: polymer is varied depending on the size and shape of the tablet, on the drug amount and drug release rate, and depends also on the molecular weight and viscosity grade of the polymer ..." (Col. 9, lines 28-34).
- The polymeric matrix of the drug delivery may also contain a hydrophobic polymer such as ethylcellulose and methacrylic acid derivatives (Col. 9, lines 45-52).
- The hydrophobic polymer is added to the hydrophilic polymer in amount from about 0.1 to about 10%, preferably from about 1% to about 5%, of the total polymer. Ratios of hydrophilic to hydrophobic polymer are from about 99.9:0.1 to about 90:10, preferably from about 99:1 to about 95:5 (Col. 9, lines 63-65).
- Tablets that may be coated with pharmaceutically acceptable coatings are disclosed (Col. 10, lines 60-67).

- The carbamazepine derivative is delivered once a day (Col. 11, lines 31-32).

It is well settled that "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." MPEP § 2131 (quoting *Verdegaal Bros. v. Union Oil Co. of Calif.*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987)). "The identical invention must be shown in as complete detail as is contained in the . . . claim." *Id.* (quoting *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989)). Therefore, Katzhender must describe each and every element of the claims in order to anticipate under Section 102(b).

Applicant respectfully submits that, contrary to the Examiner's statement, Katzender does not teach each and every element of Applicant's claims as amended. More specifically, Katzender does not teach an oral dosage form of oxcarbazepine which can be administered once per day and which produces constant plasma levels of the monohydroxy derivate of oxcarbazepine (10,11-dihydro-10-hydroxy-5H-dibenz[b,f]azepine-5-carboxamide, referred to as MHD) over a twenty-four (24) hour period.

"Zero-order kinetics" mentioned in Katzender does not teach constant-plasma levels of monohydroxy derivate over 24 hours. Zero-order kinetics simply means the rate of reaction is a constant. When the limiting reactant is consumed, the reaction stops (but the reaction could proceed for an indeterminate amount of time). There is no teaching in Katzender that kinetics occur over and up to 24 hours. Also, once a day is not the same as constant level in plasma over 24 hours.

Applicant has canceled Claim 1, added new independent Claim 18, and amended Claims 4, 6 and 13. Claims 4, 6, and 13, as amended, more clearly state that the oral dosage form of oxcarbazepine which can be administered once per day produces constant plasma levels of MHD over a twenty-four (24) hour period. Therefore, as amended, Katzhendler cannot anticipate Claims 4, 6 and 13 under 35 U.S.C. § 102(b), and Applicant respectfully requests that the rejection under Section 102 is overcome.

II. Rejection of Claims 3, 4 and 9 under 35 U.S.C. § 102(b)

Claims 3, 4 and 9 are rejected by the Examiner under 35 U.S.C. § 102(b) as being anticipated by Bourquin et al. (US 5,695,782). For the reasons discussed below, Applicant respectfully submits that the rejection is overcome.

The Examiner cites Bourquin for teaching the following:

- A tablet core comprising a dosage unit of oxcarbazepine (10,11-dihydro-10-oxo-5H-dibenzo[b,f]azepine-5-carboxamide). The cellulose ether hydroxypropyl methyl cellulose disclosed as a component in a hydrophilic, permeable inner layer and in a hydrophilic, permeable outer layer (Col. 4, line 64 to Col. 5, line 40, Example 1).
- Microcrystalline cellulose is disclosed as the filler (Col. 5, line 22).

It is well settled that "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." MPEP § 2131 (quoting *Verdegaal Bros. v. Union Oil Co. of Calif.*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987)). "The identical invention must be shown in as complete detail as is contained in the . . . claim." *Id.* (quoting *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989)). Therefore, Bourquin must describe each and every element of the claims in order to anticipate under Section 102(b).

Applicant respectfully submits that, contrary to the Examiner's statement, Bourquin does not teach each and every element of Applicant's claims as amended. More specifically, Bourquin does not teach an oral dosage form of oxcarbazepine which can be administered once per day and which produces constant plasma levels of the monohydroxy derivate of oxcarbazepine (10,11-dihydro-10-hydroxy-5H-dibenz[b,f]azepine-5-carboxamide, referred to as MHD) over a twenty-four (24) hour period. Bourquin describes an immediate-release-dosage formation, because the formulation disclosed therein is essentially hydrophilic, and would dissolve in an aqueous environment.

Applicant has canceled Claim 3, added new independent Claim 18, and amended Claims 4 and 9. Claims 4 and 9, as amended, more clearly state that the oral dosage form of oxcarbazepine which can be administered once per day produces

constant plasma levels of MHD over a twenty-four (24) hour period. Therefore, as amended, Bourquin cannot anticipate Claims 4 and 9 under 35 U.S.C. § 102(b), and Applicant respectfully requests that the rejection under Section 102 is overcome.

III. Rejection of Claims 3, 4 and 9 under 35 U.S.C. § 102(b)

Claims 3, 4 and 9 are rejected by the Examiner under 35 U.S.C. § 102(b) as being anticipated by Schlütermann (WO 98/35681). For the reasons discussed below, Applicant respectfully submits that the rejection is overcome.

The Examiner cites Schlütermann for teaching the following:

- A tablet core with oxcarbazepine, microcrystalline cellulose (AVICEL PH 102) and hydroxypropyl methyl cellulose (Page 10, Example 1).

It is well settled that "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." MPEP § 2131 (quoting *Verdegaal Bros. v. Union Oil Co. of Calif.*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987)). "The identical invention must be shown in as complete detail as is contained in the . . . claim." *Id.* (quoting *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989)). Therefore, Schlütermann must describe each and every element of the claims in order to anticipate under Section 102(b).

Applicant respectfully submits that, contrary to the Examiner's statement, Schlütermann does not teach each and every element of Applicant's claims as amended. More specifically, Schlütermann does not teach an oral dosage form of oxcarbazepine which can be administered once per day and which produces constant plasma levels of the monohydroxy derivate of oxcarbazepine (10,11-dihydro-10-hydroxy-5H-dibenz[b,f]azepine-5-carboxamide, referred to as MHD) over a twenty-four (24) hour period.

Applicant has canceled Claim 3, added new independent Claim 18, and amended Claims 4 and 9. Claims 4 and 9, as amended, more clearly state that the oral dosage form of oxcarbazepine which can be administered once per day produces constant plasma levels of MHD over a twenty-four (24) hour period. Therefore, as

amended, Schlütermann cannot anticipate Claims 4 and 9 under 35 U.S.C. § 102(b), and Applicant respectfully requests that the rejection under Section 102 is overcome.

IV. Rejection of Claims 3, 4 and 9 under 35 U.S.C. § 102(b)

Claims 3, 4 and 9 are rejected by the Examiner under 35 U.S.C. § 102(b) as being anticipated by Lang (WO 01/32183). For the reasons discussed below, Applicant respectfully submits that the rejection is overcome.

The Examiner cites Lang for teaching the following:

- A tablet core with oxcarbazepine, microcrystalline cellulose and hydroxypropyl methyl cellulose (Cellulose HPM 603) (Page 13, lines 1-3 and Example 1).

It is well settled that "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." MPEP § 2131 (quoting *Verdegaal Bros. v. Union Oil Co. of Calif.*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987)). "The identical invention must be shown in as complete detail as is contained in the . . . claim." *Id.* (quoting *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989)). Therefore, Schlütermann must describe each and every element of the claims in order to anticipate under Section 102(b).

Applicant respectfully submits that, contrary to the Examiner's statement, Lang does not teach each and every element of Applicant's claims as amended. More specifically, Lang does not teach an oral dosage form of oxcarbazepine which can be administered once per day and which produces constant plasma levels of the monohydroxy derivate of oxcarbazepine (10,11-dihydro-10-hydroxy-5H-dibenz[b,f]azepine-5-carboxamide, referred to as MHD) over a twenty-four (24) hour period.

Applicant has canceled Claim 3, added new independent Claim 18, and amended Claims 4 and 9. Claims 4 and 9, as amended, more clearly state that the oral dosage form of oxcarbazepine which can be administered once per day produces constant plasma levels of MHD over a twenty-four (24) hour period. Therefore, as

amended, Lang cannot anticipate Claims 4 and 9 under 35 U.S.C. § 102(b), and Applicant respectfully requests that the rejection under Section 102 is overcome.

V. Rejection of Claims 5, 7, and 10-12 under 35 U.S.C. § 103(a)

The Examiner has rejected claims 5, 7, and 10-12 as being unpatentable over Katzhendler et al. (US 6,296,783). The teaching of Katzhendler is stated above in Section I.

In making the 103(a) rejection, the Examiner discusses that it would have been obvious to one of ordinary skill in the art to make a sustained release tablet of oxcarbazepine with HPMC and ethyl cellulose and to modify the weight ratio or total HPMC to oxcarbazepine and the weight ratio of total ethyl cellulose to oxcarbezepine during the process or routine optimization, with a reasonable expectation of producing a once a day table for delivering oxcarbazepine.

As discussed previously above, Katzender does not teach an oral dosage form of oxcarbazepine which can be administered once per day and which produces constant plasma levels of the monohydroxy derivate of oxcarbazepine (10,11-dihydro-10-hydroxy-5H-dibenz[b,f]azepine-5-carboxamide, referred to as MHD) over a twenty-four (24) hour period. In view of Applicant's amendments, claims 5, 7, and 10-12 all depend on claim 2.

Katzender also does not expressly teach the weight ratio of total HPMC to oxcarbezepine from about 1:10 to 1:20 or the weight ratio of total ethyl cellulose to oxcarbezepine from about 1:10 to 1:20. In fact, the the most preferable polymer to drug ratios disclosed in Katzender are from 10:90 to about 80:20, which are outside the present invention and teach away from the weight ratio claimed by the Applicant. Applicant respectfully submits that it would not therefore have been obvious to one of ordinary skill in the art at the time the invention was made to modify the weight ratio to those claimed by the Applicant.

Here, Applicant has surprisingly found, after exhaustive testing, an oral dosage form of oxcarbazepine which can be administered once per day and which produces constant plasma levels of the monohydroxy derivate of oxcarbazepine (10,11-dihydro-

10-hydroxy-5H-dibenz[b,f]azepine-5-carboxamide, referred to as MHD) over a twenty-four (24) hour period. Applicant respectfully asserts that one skilled in the art would not be led from the delivery system disclosed by Katzender because the modified release formulation discovered by Applicant was the product of exhaustive testing.

Applicant has canceled Claims 5 and 7 and amended Claims 10 through 12. For the reasons stated above, Katzender fails to teach or suggest the required elements of Applicant's claimed invention, and Applicant respectfully requests that the rejection under 35 U.S.C. § 103(a) is therefore overcome.

VI. Rejection of Claim 8 under 35 U.S.C. § 103(a)

The Examiner has rejected claim 8 as being unpatentable over Katzhendler et al. (US 6,296,783) in view of Eibl (US 5,290,769). The teaching of Katzhendler is stated above in Section I. The Examiner cites Eibl for teaching tablet dosage forms (Col. 2, lines 1-2) and coating substances including copolymerizates of acrylic and methacrylic acid esters and trimethylammonium methacrylate (Col. 6, lines 23-25).

In making the 103(a) rejection, the Examiner discusses that it would have been obvious to one of ordinary skill in the art to make a sustained release tablet, with methacrylic acid derivatives, as suggested by Katzhendler, and combine it the copolymerizates of acrylic and methacrylic acid esters and trimethyammonium methacrylate, as suggested by Eibl, with a reasonable expectation of producing a sustained release tablet of oxcarbazepine.

Applicant respectfully submits that neither Katzender nor Eibl teach an oral dosage form of oxcarbazepine which can be administered once per day and which produces constant plasma levels of the monohydroxy derivate of oxcarbazepine (10,11-dihydro-10-hydroxy-5H-dibenz[b,f]azepine-5-carboxamide, referred to as MHD) over a twenty-four (24) hour period. Applicant submits that Claim 8 depends on claim 2, and that claim 1 has been withdrawn.

Katzender also does not expressly teach the weight ratio of total HPMC to oxcarbezepine from about 1:10 to 1:20 or the weight ratio of total ethyl cellulose to oxcarbezepine from about 1:10 to 1:20. In fact, the the most preferable polymer to drug

ratios disclosed in Katzender are from 10:90 to about 80:20, which are outside the present invention and teach away from the weight ratio claimed by the Applicant. Applicant respectfully submits that it would not therefore have been obvious to one of ordinary skill in the art at the time the invention was made to modify the weight ratio to those claimed by the Applicant.